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105 Omalizumab – a treatment option against incipient allergic bronchopulmonary aspergillosis when combined with severe allergic asthma and diabetes mellitus

P. Meyer[1]. [1]Pediatrics, University Hospital, Lund, Sweden

Objectives: Cystic fibrosis (CF) patients are at risk for being colonized in their lungs not only by bacteria but also moulds. *Aspergillus fumigatus* (Af) colonization can lead to allergic sensitization against Af and severe bronchial obstruction known as allergic bronchopulmonary aspergillosis (ABPA). The recommended treatment against ABPA is systemic corticosteroids (CS) but is difficult to use with concomitant diabetes mellitus (DM). An alternative treatment is needed.
Methods: A 9 year old girl suffering from CF, DM, coeliac disease, severe allergic asthma and incipient ABPA. Her asthma was poorly controlled in spite of modern anti-asthma treatment including high dose inhaled CS and her lung function deteriorated. Immunological markers for ABPA: Total IgE and specific IgE were both doubled in one year to 747 kU/L and 19.2 kU/L and recombinant Asp f 4 was 7.72 kU/L (ImmunoCAP). All together she was judged as incipient ABPA. She started treatment with omalizumab, a humanized monoclonal anti-IgE antibody, known to be effective against severe uncontrolled allergic asthma.
Results: She has achieved good asthma control. Serological ABPA-markers has not increased and lung function is stable. The treatment has been without side effects.
Conclusion: Omalizumab is a treatment option against incipient ABPA, especially when combined with DM.

106 Direct dispensing of dornase alfa improves adherence and lung function in cystic fibrosis (CF)

M. Hagelberg[2,1], M.J. Dooley[2], S.G. Poole[2], D. Leung[2], M. Bailey[1], F. Finlayson[1], D. Clark[1], M. Braithwaite[1], T. Kotsimbos[1], J.W. Wilson[1]. [1]CF Service, Alfred Hospital, Melbourne, VIC, Australia; [2]Pharmacy, Alfred Hospital, Melbourne, VIC, Australia

Background: Non-adherence to treatment plan is a recognised problem in CF. Dornase alfa (DA) has been shown to improve outcomes in cystic fibrosis.
Aim: To assess direct dispensing as an adherence-improving intervention and compare dispensing rates and health outcomes to those with no intervention.
Method: Recruited patients were randomised to either direct dispensing (DD) i.e. DA was given directly to patients in clinic or self-dispensing (SD) i.e. patients volitionally went to pharmacy. The study period was 6 months. Records were retrospectively accessed to determine outcomes in dispensing rates, FEV1, FVC and BMI. Dispensing rate was used as an index of adherence.
Results: Twenty patients in the DD-group had a significantly improved ($p = 0.001$) dispensing rate from 71% during the past 6 months to 106% during the 6 months study period. After the intervention their pick-up rate decreased ($p = 0.050$) to 82%. The DD-group had a significantly higher dispensing rate ($p = 0.033$) than the 19 patients in the SD-group during the study period. There was no significant difference in pick-up of DA in the SD-group over time. Subjects in the DD-group had a significantly less decline FEV1 from baseline over 300 days from the start of the study compared to the SD-group. There was no significant difference in FVC or BMI between the groups.
Conclusion: Direct dispensing of DA significantly improves pick-up rate and FEV1. Further investigations are required in terms of behavioural changing interventions to improve adherence long-term. Studies with larger groups are needed to identify any correlation between improved pick-up rate and health outcomes.
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107* Sinu-nasal inhalation of Dornase alfa in CF. Results of a double-blind placebo-controlled pilot trial

J. Mainz[1], H.J. Mentzel[2], G. Schneider[3], J. Riethmuller[4], I. Schiller[1], C. Ritschel[1], J.F. Beck[1], B. Wiedemann[5]. [1]Pediatrics, University, Jena, Germany; [2]Radiology, University, Jena, Germany; [3]Otorhinology, University, Jena, Germany; [4]Pediatrics, University, Tubingen, Germany; [5]Biometrics, University, Dresden, Germany

The paranasal sinuses are almost regularly involved in CF. Therefore, chronic rhinosinusitis (CRS) and nasal polyposis are hallmarks of the disease.
Recombinant Dornase alfa (rhDNase) evidently improves pulmonary outcome in CF. Up to now, inhalative drug deposition into paranasal sinuses was substantially limited. The novel Pari-Sinus device was shown to deliver aerosol into this segment in cast-models and recent human scintigraphic deposition-studies.
The present DBPC cross-over pilot-trial is the first clinical study with the device. It was performed to evaluate primary outcome parameters and patient numbers needed for a consecutive main study. Parameters were changes in CRS-related quality-of-life (Sino Nasal Outcome-Test = SNOT-20) and in sinu-nasal Magnet Resonance Imaging (MRI).
Five CF patients with CRS were included from the Jena University-CF-centre. For each 28 days they inhaled rhDNase and NaCl0.9%, with an intermediate wash-out-period.
Whereas placebo did not lead to comprehensible changes of SNOT-20-overall scores, rhDNase led to a reduction of symptoms ($p < 0.05$). Most pronounced results were found regarding verum-effects on factors like nasal secretion and obstruction. In contrast, MRI results scattered widely without any trend. These limitations of sinunasal imaging may be caused by the nasal cycle: nasal blood circulation alternates congested and decongested sides every 2–6 hrs.
Although the small cohort does not allow assignment of statistical significance, promising trends are given for effectiveness of rhDNase-nebulization with the novel device.
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108 Colistin CF for aerosol therapy of the upper airways – An in-vitro deposition study with the PARI SINUS

U. Schuschnig[1], E. Klopfer[1], A. Krüner[1], R. Schmid[2], M. Keller[1]. [1]PARI Pharma GmbH, Munich, Germany; [2]Grünenthal GmbH, Aachen, Germany

Introduction: Recent studies show that the upper airways are colonized with bacteria of the same genotypes as found in the lower airways, indicating that a comprehensive treatment of upper and lower airways is desirable.
This study was conducted with Colistin CF aerosolised by the SINUS pulsating delivery system in order to estimate how much of the drug deposits in the nasal and paranasal cavities.
Methods: Nebulization efficiency was investigated using a nasal cast model. This cast is based on anatomical dimensions and is equipped with two cavities (sinuses), each in frontal, maxillary and sphenoid position. The ostium/volume configuration of the sinuses in this study was as follows: frontal 0.5mm/7.5 ml, maxillary 2mm/23 ml and sphenoid 1mm/12.5 ml.
Nebulisation of 3 ml Colistin solution (79 mg colistimethate sodium/3 ml) was conducted for 5 minutes first into the left then 5 minutes into the right nostril of the model, while the opponent nostril was equipped with a filter. After the experiment the nasal cast model was dismantled and drug extracted with solvent from the paranasal cavities, the ostia, the nasal cavity, as well as from the nebuliser and the filter. Colistin content of these solutions was assayed by HPLC a Corona detector.
Results: After nebulization, about 4% of the Colistin dose loaded in the nebulizer was found in all six sinus cavities. Deposition in the single sinus cavities ranged from 0.3‰ (frontal) up to 1.4% (maxillary). 51% of the initial drug charge remained in the nebulizer while 6% were found in the nasal cavity and 34% were found on the exit filter.
Conclusions: PARI SINUS can deliver nebulised Colistin CF via it's pulsation mode to all sinus cavities of a nasal cast model, even when the ostium diameter is only 0.5 mm.